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Brief descriptive runninghead: Micro-ureteroscopy to treat pelvic stones in women

Abstract:

Purpose: The aim of this study is to assess the effectiveness, safety and reproducibility of the micro - ureteroscopy (m - URS) in the treatment of distal ureteral stones in women.

Materials and Methods: A multicenter, prospective, observational study was designed and conducted between March and December 2015. We included women having at least one stone in the distal ureter and being a candidate for surgical treatment employing the 4.85 French sheath of Micro-Perc®. Patients with clinical criteria and/or laboratory analysis indicating sepsis, or coagulation alteration were excluded.

Results: 39 women were operated in 8 hospitals. The profile of the patients was fairly homogeneous among hospitals. Only differences were found in age, preoperative stent and the result of the previous urine culture. Immediate stone-free status was achieved in 88.2% and 100% seven days after the procedure. 97.4 % of patients did not present any complication in the postoperative period, with only one case with complication Clavien II. PULS (Post-Ureteroscopic Lesion Scale) scale in 76.9 % of patients did not show any injury, 20.5% had lesions grade 1 and grade 2 lesions 2.6 %. As for the reproducibility of micro - ureteroscopy between hospitals, statistical analysis of the results showed differences between all the centers participating in the study.

Conclusions: Micro-ureteroscopy is an effective, safe and reproducible technique that minimizes surgical aggression to the ureteral anatomy. Satisfactory and comparable results to "conventional" ureteroscopy were obtained in the treatment of distal ureteral stones in women, though clinical trials are needed. The reduction of the ureteral damage may reduce secondary procedures and increase the cost-effectiveness of the procedure.

Brief descriptive runninghead: Micro-ureteroscopy in the treatment of stones in women

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Key words: Miniaturization; Minimally Invasive Surgical Procedures; Ureteroscopy; Urinary Calculi; Reproducibility of Results

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Materials and Methods: A multicenter, prospective, observational study was designed and conducted between March and December 2015. We included women having at least one stone in the distal pelvic ureter and being a candidate for surgical treatment employing the 4.85 French sheath of Micro-Perc®. Patients with clinical criteria and/or laboratory analysis indicating sepsis, or coagulation alteration were excluded.

Results: 39 women were operated in 8 hospitals. The profile of the patients was fairly homogeneous among hospitals. Only differences were found in age, preoperative stent and the result of the previous urine culture. Immediate stone-free status was achieved in 88.2% and 100% seven days after the procedure. 97.4 % of patients did not present any complication in the postoperative period, with only one case with complication Clavien II. PULS scale(Post-Ureteroscopic Lesion Scale) scale in 76.9 % of patients did not show any injury, 20.5% had lesions grade 1 and grade 2 lesions 2.6 %. As for the reproducibility of micro - ureteroscopy between hospitals, statistical analysis of the results showed statistically significant differences between all the centers participating in the study.

Conclusions: Micro-ureteroscopy is an effective, safe and reproducible technique that minimizes surgical aggression to the ureteral anatomy. Satisfactory and comparable results to “conventional” ureteroscopy results that wereare comparable to “conventional” ureteroscopy wereare obtained in the treatment of pelvic distal ureteral stones in women, though clinical trials are needed. The reduction of the ureteral damage may reduce secondary procedures and increase the cost-effectiveness of the procedure.

Title: Assessment of the effectiveness, safety and reproducibility of micro-ureteroscopy in the treatment of distal ureteral stones in women: a multicenter, prospective study.

Introduction:

Various factors explain the increase in the prevalence of urinary stone disease both in Spain and in other areas of Europe and the World[1]. There is also an increase in the direct and indirect spending expenses generated by this disease[2].

Ureteral stones generate the greatest morbidity. In these cases, tThe therapeutic options are to initiate medical treatment with the objective of spontaneous passage of the stone, medical expulsive therapy (MET), or to start active treatment, either with through extracorporeal shock wave lithotripsy (ESWL) or ureteroscopy (URS). AltThough medical expulsive therapyMET appears to be the most attractive option[3], as the least interventional of all, its efficacy mightaybeis limited[34] even in stones smaller than 10 mm. Therefore, active treatment options for ureteral lithiasis are growing in popularity.

The objective of ESWL is the external fragmentation of the stone, with the hope thatso the smaller fragments can then be spontaneously passed spontaneously by the patient. In the specific case of URS, the fragmentation or pulverization of the stone fragmentation occurs directly in the ureter, and its extraction is immediate. This is the primary advantage of URS over ESWL, at the expense of higher morbidity[45]. One of the major advances in endourology in order to reduce iatrogeny while maintaining efficacy, is the miniaturization of the endoscopic instruments. The use of smaller-calibrer ureteroscopes reduces ureteral damage, the risk of complications and the need for post-operative catheterization, thereby improving the patient's quality of life after the procedure[5-6-7]. In 2015, in this line of research, weour group published ourits first experience inwith the treatment of pelvic distal ureteral lithiasis in women using micro-ureteroscopy (m-URS) through with the retrograde use of the 4.85 Fr.[78]sheath from the micro-percutaneous (micro-PERC®) surgery set[89].

The aim of this study is to evaluate the effectiveness, safety and reproducibility of this technique in the treatment of pelvic distal ureteral stones in women.

Materials and methods:

Study design:

A multicenter, prospective, observational study was designed and conducted between March and December 2015. The inclusion criteria were: being woman over 18 years of age, having at least one stone of any size in the distal pelvic ureter and being a candidate for surgical treatment according to the standard practice of each site, either scheduled or as an emergency. Patients with clinical criteria and/or analitycal laboratory analysis indicating sepsis criteria, patients with an irreversible coagulation clotting alterationdisorder, or patients who would not sign the informed consent to undergo the procedure were excluded. The ethical principles and recommendations of the Declaration of Helsinki were respected during this research.

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The participating sites were IMQ Zorrotzaurre Clinic (Bilbao, Spain), Santiago de Compostela Universitary Hospital (A Coruña, Spain), Universitary General Hospital of Alicante (Alicante, Spain), La Paz Universitary Hospital (Madrid, Spain), La Fe Universitary and Politechnic Hospital (Valencia, Spain), La Ribera Universitary Hospital (Alzira, Spain), Rio Hortega Universitary Hospital (Valladolid, Spain) and Universitary Hospital of Vinalopo (Elche, Spain). 8 surgeons from different centers participated in the study. To achieve the objectives, bBetween 4 and 5 operations were performed atin each center.one of the 8 participating hospitals. Three of the eight study surgeons had prior experience in micro-ureteroscopy ranging from 5 to 10 cases each. The rest understood the material used and attended a workshop to learn the technique.

Surgical technique:

The 4.85 Fr. sheath from the Micro-Perc® set and the 10,000 pixel, 120 degrees, 0.9 mm diameter flexible optic system (Polydiagnost, Germany) (see Figures 1 and 2) were used for m-URS. A 3-arm luer lock adapter was connected to the sheath to insert the optics (through the middle arm), the irrigation (either with perfusion pump or gravity dripping) through one lateral arm, and the 230 laser fiber through a Tuohy Borst Adapter (Cook®, USA) to avoid irrigation dripping through the third arm.

The use of accessory materials (safety guidewire or 1.3 Fr. stone-basket), antibiotic prophylaxis protocols, anaesthesia techniques or the decision to insert a stent prior to surgery or afterwards was left to the surgeons' criteria, according to their standard practice. Most of the times the sheath iswas inserted retrogradly in the ureter with neither need of meatus dilation nor safety guidewire.The entire procedure was performed under endoscopic vision (see Figure 3). Laser settings were adjusted to dust the stone and try avoiding the need for fragments removal.

In those cases, in which the surgeon observed difficulty in completely treating the stone with m-URS, the conventional ureteroscope could be used. We defined a "conventional" ureteroscope as that not designed "a priori" for use in pediatric patients (i.e. tip diameter greater than 7.5 Fr).

The material used for the micro-ureteroscopy was the 4.85 Fr. sheath from the Micro-Perc® set (Polydiagnost) and the 10,000 pixel, 120 degrees, 0.9 mm diameter flexible optic system (see Figures1 and 2). In those cases, in which the surgeon observed difficulty in completely treating the lithiasis through micro-ureteroscopy, the conventional ureteroscope could be used. We define a "conventional" ureteroscope as that not designed "a priori" for use in pediatric patients, for which reason it has a tip diameter greater than 7.5 Fr.

The 4.85 Fr. sheath is connected to the 3-Luer-Lock adapter. The 0.9 mm optic is inserted through the middle channel of the adapter. A Touhy Borst Adapter (Cook®, USA) is connected to a second channel, the laser fiber is inserted through this channel. Finally, the irrigation is connected to the third channel. Most of the times the sheath is placed retrogradly in the ureter with no need of meatus dilation and no need of safety guidewire. We performed the entire procedure under direct vision.

The saline infusion method was used with a perfusion pump or gravity drip, as per the site. The use of accessory materials (safety guidewire or 1.3 Fr. stone-basket), antibiotic prophylaxis protocols,

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anaesthesia techniques or the decision to insert a stent prior to surgery or afterwards was left to the surgeon's criteria, according to his or her standard practice.

Laser settings were adjusted to pulverize the stone and avoid the need of removing fragments.

Study variables:

The independent variables consisted of the following data: age, sex, body mass index (BMI), diabetes history, use of antiplatelet or anticoagulant drugs, ASA classification, possible genitourinary malformations, characteristics of the stones, previous treatments for ipsilateral lithiasis and the result of the previous culture.

The primary endpoints are encompassed under the study objectives: The **effectiveness** of the procedure was assessed through the number of immediately stone-free cases as observed through endoscopic and/or fluoroscopic study (see Figure 4) after the procedure, and 7 days after the intervention through KUB x-ray of the abdomen. The **safety** of the technique was evaluated through the incidence of complications, using the modified Clavien-Dindo scale, and through the analysis of any ureteral damage caused, with the Post-Ureteroscopic Lesion Scale, or PULS. In all cases a renal ultrasonography and/or a computed tomography waswere performed 3 to 6 months after the procedure.

Other variables were the use or not of cystoscope, safety guidewires, "conventional" ureteroscope or urinary catheter during the procedure. The duration of the intervention and the need to convert the procedure to conventional ureteroscopy, as well as the reason, the need to use post-operative ureteral stent, and its duration were also recorded.

Statistical analysis:

The primary study variables were summarized using means as measures of central tendency and the 95% confidence interval (CI95%) as measure of dispersion for the quantitative variables, and frequencies and percentages for the qualitative measures.

For the study of the **reproducibility or homogeneity** of the procedure, percentages were calculated for the qualitative variables for each one of the hospitals. To discuss the possible differences between the hospitals, the non-parametric statistics Chi-Square Distance, symmetrical Lambda and the Goodman-Kruskal Tau were calculated. In the case of quantitative variables, medians per hospital were calculated. The non-parametric Kruskal-Wallis (KW) statistic was used to obtain possible differences between hospitals, in addition to the parametric, single-factor ANOVA procedure. The statistical package used was the SPSS 15.0 program.

The lack of data per hospital can call into question the assumptions of normality and homoscedasticity, but not independence, for the application of ANOVA, though the solidity of the method in the face of this lack of homoscedasticity of requirements is known in cases where the sample size from each hospital is practically equal.

To perform the analysis of the homogeneity of the results between the different hospitals, the sites that were required to use the cystoscope to remove a ureteral stent prior to the current procedure were excluded. A decision was made to also exclude the site that systematically uses a safety

guidewire to perform the procedure and the site that, per protocol, leaves any ureteral stent inserted in situ for 14 days.

Results:

The demographic characteristics of the study population are reflected in Table 1. The patient profile was fairly homogeneous among the hospitals (Table 2). Differences were only observed in age, having a preoperative stent and the result of the previous culture. While in one hospital the median age was 37 years, in another, it stood at 79 years. In half of the sites, no patients had preoperative stents, while in two sites, 4 and 3 women, respectively, had preoperative stents in place. Finally, in 3 hospitals, the previous culture was negative in all cases and, in another, all of the cultures were positive.

Previous treatments included 6 ESWL performed no more than one month previous to the micro-ureteroscopy, 1 case of retrograde intrarenal surgery and a percutaneous nephrolithotomy each. Finally, in two cases an ipsilateral ureteroscopy was done more than 4 years ago and in 1 case the URS was performed 2 weeks prior m-URS.

Regarding how each surgeon's appliedpreferences for the m-URSicro-ureteroscopy technique (see Table 3), the cystoscope was chosen in 2 of the 27 cases not previously having a bearing double-J stent. In 94.3% (86.6%-100%) the meatus was accessed directly, with no safety guidewire. In 4 patients, 10.3% (0.8-19.8%) of the total, the conventional ureteroscope had to be used. The reasons for using the ureteroscope were, in 3 cases, poor image quality and, in 1 case, the inability to mobilize an impacted stone using the m-URS equipment. In no case was it necessary to convert due to stone retropulsionmigration of the stone to a level of the ureter where, due to the sheath´sits length, the stone was not accessiblereachablesheath of the m-URS could not access.

In 35 patients (89.7%) of cases, the stone was fragmented dusted using the Holmium laser. In 6 renal units, a double-J stent was inserted and, in 5, an external straight ureteral stentrectal ureteral stent was inserted for 24 hours. The ureteral stents were maintained for a mean of 3.5 days. The mean duration of the surgery was 35.8 minutes (CI95% 29.3-42.2).

In terms of the effectiveness of m-URS, 30 patients (88.2%) were stone-free immediately and 100% were stone-free one week after the procedure. No retreatment was required in any case.

Regarding the safety of the technique, 97.4% of the patients presentshowed no problems of any kind during the postoperative period, with a single case with Clavien II complication. On the PULS scale, 76.9% of patients did not present any lesion, 20.5% presented grade 1 lesions and 2.6% presented grade 2 lesions. The renal ultrasonography and/or the computed tomography performed 3 to 6 months after the procedure demonstrated no hydronephrosis.

With respect to the reproducibility of the micro-ureteroscopy between among hospitals, the results analysis for the intervention revealed no statistically significant differences between the sites participating in the study (Table 4). Moreover, no differences were found between novel and experienced surgeons (Table 1 and 3).

Discussion:

According to the American Urological Association (AUA) and the European Association of Urology (EAU) guidelines, patients with ureteral stones under 6 mm, or even under 10 mm, can be offered conservative medical management provided there are no complication criteria[9,10,11].

Male patients were excluded from this study since the urethral length and its curve at the prostate levelanatomy limit the instrumentation with the micro-ureteroscopy sheath, with its reduced length (22.5 cm) and caliberre. The upper limit in women is L5-S1 level, in men the limit is being the sciatic spine and, in children, according to the age we can even reach the renal pelvis. With respect to the characteristics of the patients Patients treated, the age was higher than in the majority of the studies consulted[1112]. The level of comorbidity and body mass index (BMI) wereas comparable to that of other series.

With respect to the results of the micro-ureteroscopy, tThe surgical time in our study with micro-ureteroscopy (35.8 minutes) was shorter than that published by the CROES with "conventional" ureteroscopy (42.2 min). This couldcan be explained by a smaller mean surface area of the stones treated in our series (33.3 mm^2 versus 66.6 mm^2)[1213].

Except forin those patients with ureteral stent prior to the intervention or in the cases in which safety guidewires were used per protocol, the use of a cystoscope was only required in two cases to perform the micro-ureteroscopy. Therefore, with respect to standard practice, in these specific cases, m-URS could involve an increase of instrumentation. used versus ureteroscopy.

AltThough guidelines recommend the use of safety guidewires[9,10,11], some authors have already published studies comparingpreviously compared the complications with and without their use[1314]. In our study, each surgeon was free to use a safety guidewirethem or not. This Guidewires could be inserted through the very 4.85 Fr. sheath with fluoroscopic guidance or prior to the insertion of the sheath with a cystoscope. In this study, tThe meatus was accessed with no guidewire in 85% of all cases. One of the sites decided to follow the recommendations of the guidelines and employed the safety guidewire in 75% of its cases. In the rest of the sites, only 2 surgeons, in 1 procedure each, observed a need to use the safety guidewire it during the treatment of the stone.

The reduced diameter of the sheath makes the distance between it and the ureteral wall greater. Therefore, the risk of damaging the meatus or the intramural ureter could be lower with m-URS.

The micro-ureteroscopy sheath only allows us to work with laser fibers between 230 and 270 microns (classic tip, not round), while "conventional" ureteroscopy allows for the use of wider fibers with a greater calibre. The existing studies are not conclusive regarding whether or not the diameter of the fiber affects the capacity to fragment the stone[14,15,16]. In any case, we consider its performance to be sufficient to treat the lithiasis in an acceptable period of time. In the study by Galán et al.[1617] the mean surface area of the stones treated was 33 mm^2, which is very similar to ours, with a greater longer surgical time, at 42 minutes. It should be noted that the majority of the sites participating in the study were experts in ureteroscopy, but that this was their first contact with micro-ureteroscopy.

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The use of the conventional ureteroscope was due to poor image quality in 3 out of 4 cases. It is important to note that this circumstance always All of them occurred in the same site. This leads us to believe that it could be due to an isolated failure of the site's m-URS equipment.

Though there were 15 impacted stones, the use of the "conventional" ureteroscope was only required to treat the stone in one case. The frequency of impacted stones in our series (38.5%) is higher than that published by the CROES (29.2%) for distal ureter lithiasis, 38.5% in our study versus 29.2% in the CROES study[1213]. This is an independent factor for the increasinge of postoperative complications[1718].

It is remarkable that starting treatment with m-URS did not impede the successful completion of the procedure in any case. Therefore, no patients required retreatment.

In terms of About the **effectiveness** of the micro-ureteroscopym-URS, the immediate success of the treatment was homogeneous among the different sites. One of the sites did not classify any of its cases as immediately stone-free. This site considered that no patient couldan be declared stone-free right at the time the procedure is was finalized. In the rest of the hospitals, there was consensus to classify all of the patients as were stone-free 7 days after treatment. This result is in line with the results of conventional ureteroscopy in the treatment of distal ureteralpelvic ureter lithiasis[1819].

To measure the **safety** of micro-ureteroscopy, the adaptation of the Clavien-Dindo classification was used[19-2120-22] for postoperative complications. A total of 97.4% of patients did not present any complications, and there was only one case of a grade 2 complication (postoperative fever that was resolved with endovenous antibiotic treatment). The study by Pérez-Castro et al. for the Endourological Society, in which 9681 patients were included, presented 3.8% intraoperative complications and 2.4% postoperative complications for distal ureter stones.

In our case, the grade 2 complication in the Clavien Dindo scale was one case of postoperative fever that was resolved with endovenous antibiotic treatment.

Moreover, we used the PULS scale[2223], to assess ureteral damage, caused by either the surgical intervention or by the ureteral stoneinary lithiasis itself. However, the series published to date differ regarding the characteristics of the stones treated; therefore, those results are not comparable to ours[22-2423-25]. It would be advisable to reach an agreement on the adoption of this scale in results the reporting of results from different groups.

The postoperative ureteral stent is a factor that independently affects patient quality of life[25,26,27]. The study conducted by the CROES for the treatment of ureteral lithiasis, with respect to distal ureteral lithiasis, indicated that showed that a double-J ureteral stent was inserted in 54.7% of the cases[1213] despite multiple studies certifying that a ureteral stent is not to be used systematically in uncomplicated ureteroscopies[27-2928-30]. Moreover, Caballero et al. presented their results in a prospective-retrospective study and described a reduction in the insertion of ureteral stents in patients treated with micro-ureteroscopy versus patients treated with ureteroscopy using a 7.5-9.5 Fr. ureteroscope[3031]. In our casesstudy, a ureteral stent was inserted in 17.1% of the cases. This highly favorable result may be due to the smaller size of the stone treated or to the reduced size of the micro-ureteroscopy sheath; in any case, further studies are needed to make draw any conclusions in this regard.

During the study, each urologist was surgeons were able to follow his theiror her standard practice and, at one site, the duration of the ureteral catheterization was always 14 days, regardless of the degree of ureteral lesion observed. Since some authors[2223] establish that each degree of ureteral lesion requires a different duration of ureteral catheterization, this is not always possible due to the healthcare or administrative circumstances of each site.

The statistical analysis of the results by site demonstrateds the homogeneity of the micro-ureteroscopy technique. No significant differences were found in the technical variables or in the results of the technique across the hospitals participating in the study, therefore, the result could suppose the homogeneity of the micro-ureteroscopy technique..

The primary limitations of the study wereare the reduced sample size, though the multicenter nature of the study reinforces the reproducibility data found. The non-use of a standardized protocol may seem to be a limitation of this study, but in the authors' opinion, it shows that the technique is feasible regardless of the procedure used and its variations. Another limitation of the study might be the inability to determine the cost-effectiveness of the procedure. The sheath is a disposable device. Its cost is about 400 US dollars. In any case reducing the ureteral damage could reduce the readmission rate, the rate of inpatient procedures, the need of secondary procedures and/or the use of analgesics.

Conclusions:

Micro-ureteroscopy is an effective, safe and reproducible technique that minimizes surgical aggression to the ureteral anatomy. Satisfactory results that are cComparable results to "conventional" ureteroscopy are obtained in the treatment of distal pelvic ureteral stones in women, though clinical trials comparing the two techniques are needed to assess any advantages or disadvantages. The reduction of the ureteral damage may reduce secondary procedures and increase the cost-effectiveness of the procedure.

Abbreviations:

SWL: *Extracorporeal shock wave lithotripsy*

URS: Ureteroscopy

Fr.: French

m-URS: Micro-ureteroscopy

KW: Kruskal-Wallis

BMI: Body mass index

Cm: *Centimeters*

mm.: *milimeters*

min: minutes

KUB x ray: Kidney Ureter and bladder X-ray

PULS: Postureteroscopic lesion scale

CI: confidence interval

AUA: American Urological Association

EAU: European Association of Urology

CROES: Clinical research office of the endourological society

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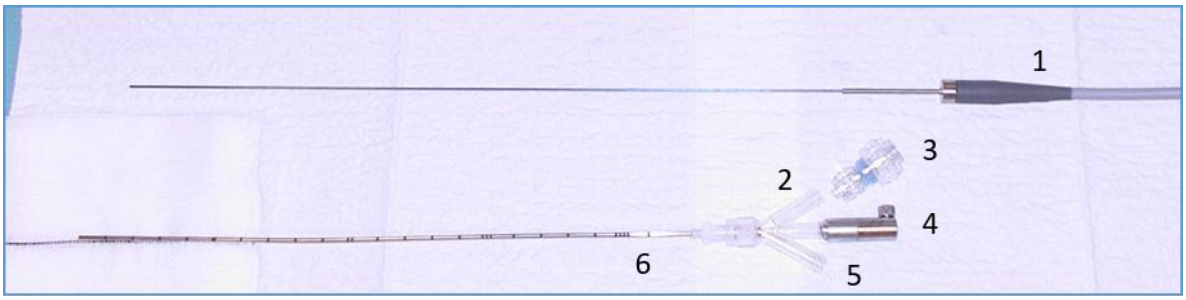

Figure 1. Equipment used in micro-ureteroscopy: 1- 0.9 mm diameter optic; 2- 3 Luer Lock adapter; 3- Tuohy Borst Adapter; 4- Optic adapter; 5- Irrigation channel; 6- 4.85F sheath of MicroPerc set.

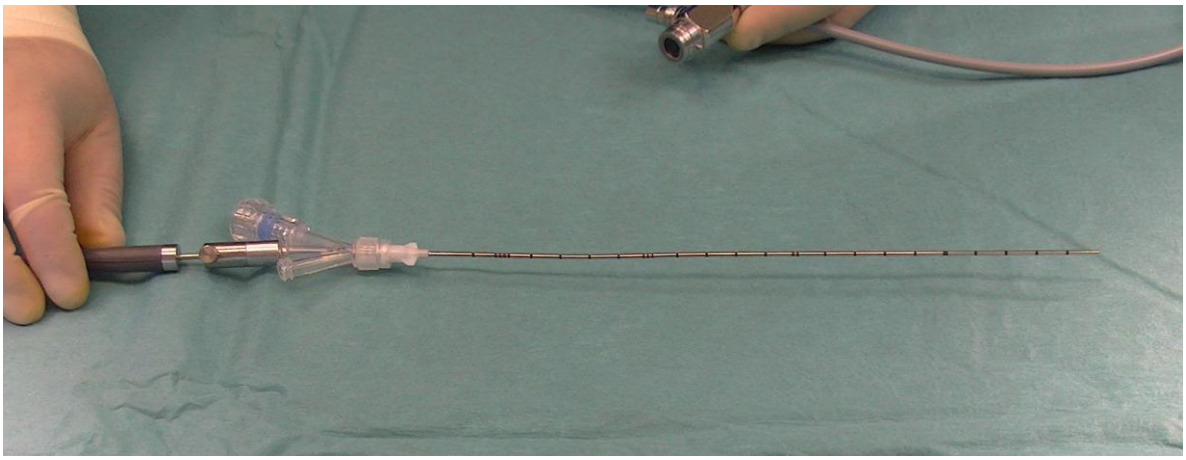

Figure 2. Material prepared for micro-ureteroscopy.

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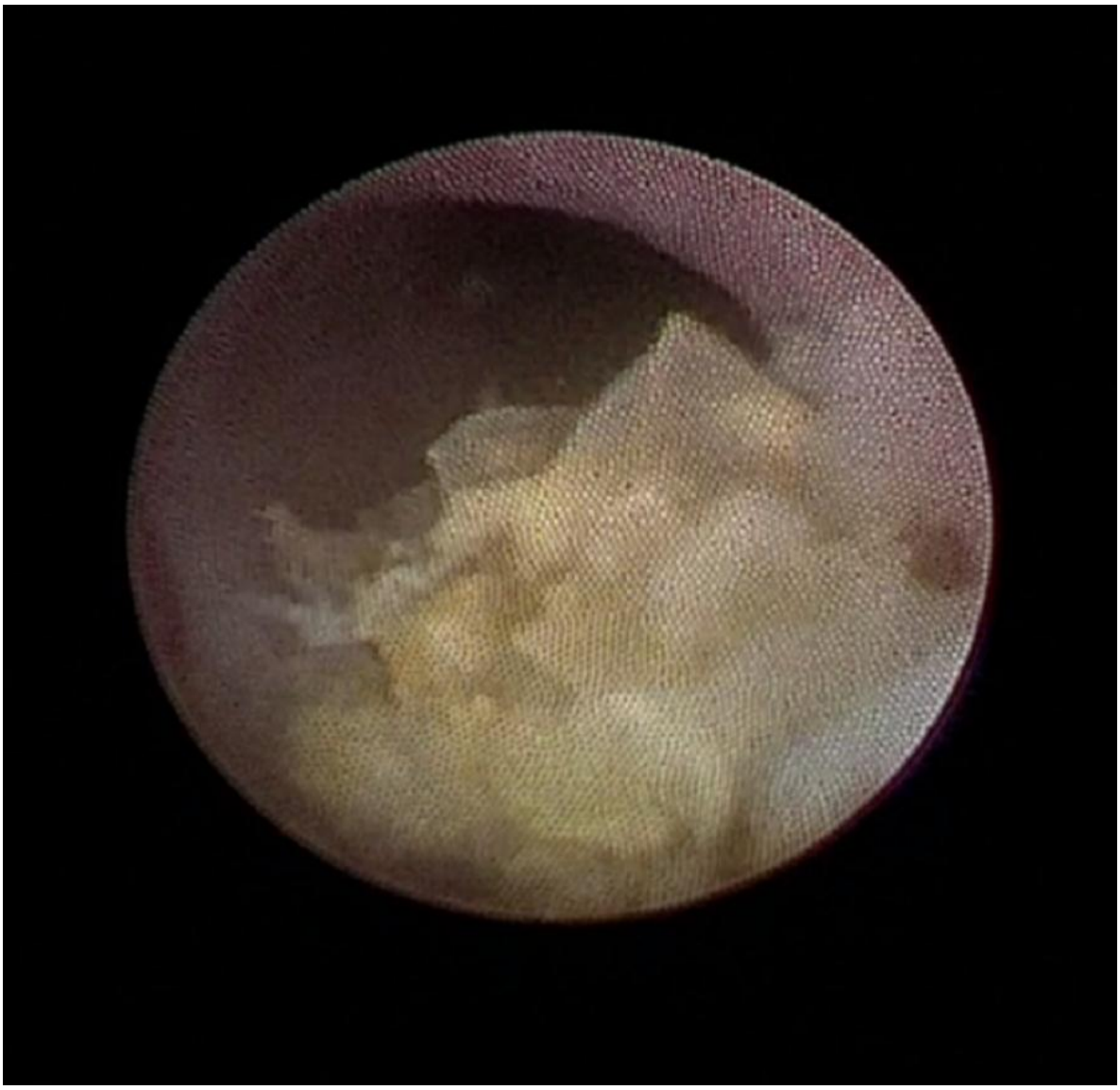

Figure 3. Endoscopic image during the procedure before starting dusting a stone.

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Figure 4. Intraoperative fluoroscopy, in which the sheath for micro-ureteroscopy is identified inside the left ureter during the treatment of a distal ureteral stone.

Table 1: Patient characteristics and analysis according to surgeons' experience

	N	Mean	n (%)	Confidence Interval 95%	Non-experienced surgeons (n = 24) N (%)	Experienced surgeons (n = 15) N (%)
Age (years old)	39	56.18		(50.9 - 61.4)	55.7¶	56.9¶
BMI (kg/m^2)	36	26.21		(24.3 - 28.1)	26.6¶	25.5¶
Diabetes	38		6 (15.8)	(4.2 - 27.4)	3 (12.0%)	3 (21.4)
Antiplatelet drugs	38		1 (2.6)	(0.0 - 7.7)	1 (4.2%)	0 (0.0)
Anticoagulant	38		1 (2.6)	(0.0 - 7.7)	0 (0.0)	1 (7.1)
ASA Classification	39					
I			12 (30.8)	(16.3 - 45.3)	9 (37.5)	3 (20.0)
II			21 (53.8)	(38.2 - 69.4)	12 (50.0)	9 (60.0)
III			6 (15.4)	(4.1 - 26.7)	3 (12.5)	3 (20.0)
Genitourinary Malformations	38		0 (0.0)	-	-	-
Side	37					
Left			17 (45.9)	(29.8 - 62.0)	11 (47.8)	6 (42.9)
Right			20 (54.1)	(38.0 -70.2)	12 (52.2)	8 (57.1)
Previous treatments of ipsilateral stones	38		11 (28.9)	(14.5 - 43.3)	8 (33.3)	3 (21.4)
Major diameter (mm.)	38	7.63		(6.6 - 8.7)	7.5	7.9
Surface of the stone (mm^2)	38	33.35		(25.1 - 41.56)	31.5	36.5
Preoperative stent	39		9 (23.1)	(9.9 - 36.3)	9 (37.5)	0 (0.0)
Impacted stone	39		15 (38.5)	(23.2 - 53.8)	8 (33.3)	7 (46.7)
Previous urinary culture	30					
Negative			23 (76.7)	(61.6 - 91.8)	15 (71.4)	8 (88.9)
Positive			7 (17.9)	(4.2 - 31.6)	6 (28.6)	1 (11.1)

BMI: body mass index; ASA: American Society of Anesthesiologists. Quantitative variables are expressed as mean and 95% confidence interval (95%), while qualitative do in frequency and percentage (%). ¶ Mean values

Table 2: Patient characteristics in each center

Hospital	A	B	C	D	E	F	G	H	X^2/gl (P-V)	λ (P-V)	τ (P-V)	K-W/gl (P-V)	ANOVA (P-V)
Age (years old (median))	37	58	79	66	68	59	43	57				11.8/7 0.107	2.12 0.07
BMI, kg/m^2 (median)	24.3	29.3	25.4	27.9	26.1	21.7	22.4	26.5				5.5/7 0.594	0.77 0.615
Diabetes	1/5	0/5	1/4	1/4	1/5	1/5	0/5	1/5	2.6/7 0.915	0.03 0.739	0.07 0.921		
Antiplatelet drugs	0/5	1/5	0/4	0/4	0/5	0/5	0/5	0/5	6.8/7 0.452	0.03 0.311	0.18 0.164		
Anticoagulant	0/5	0/5	0/5	0/4	0/5	0/5	0/5	1/5	6.8/7 0.452	0.03 0.311	0.18 0.164		
ASA Classification													
I	2/5	2/5	1/5	1/4	1/5	2/5	3/5	0/5					
II	2/5	3/5	3/5	3/4	3/5	1/5	2/5	4/5	10.6/14 0.713	0.12 0.282	0.14 0.718		
III	1/5	0/5	1/5	0/4	1/5	2/5	0/5	1/5					
Genitourinary Malformations	0/5	0/5	0/5	0/4	0/5	0/5	0/5	0/5	-	-	-		
Side													
Left	2/5	2/5	3/4	2/4	3/4	2/5	2/5	1/5	4.4/7 0.734	0.12 0.265	0.12 0.749		
Right	3/5	3/5	1/4	2/4	1/4	3/5	3/5	4/5					
Previous treatments of ipsilateral stones	0/5	3/5	1/4	0/4	1/5	2/5	2/5	2/5	7.1/7 0.416	0.09 0.278	0.188 0.435		
Major diameter (mm.(median))	6.0	7.0	10.0	5.5	8.8	6.0	7.0	7.0				6.4/7 0.498	0.95 0.487
Surface of the stone (mm^2(median))	16.5	27.5	62.8	21.6	44.0	23.6	22.0	27.5				5.4/7 0.615	1.09 0.391
Preoperative stent	0/5	1/5	0/5	1/4	3/5	4/5	0/5	0/5	19.0/7 0.008¥	0.19 0.076	0.49 0.035¥		
Impacted stone	2/5	0/5	3/5	2/4	1/5	2/5	3/5	2/5	6.0/7 0.535	0.10 0.379	0.16 0.553		
Previous urinary culture													
Negative	3/4	4/5	-/-	4/4	2/4	0/3	5/5	5/5	15.7/6 0.015¥	0.12 0.228	0.53 0.007¥		
Positive	1/4	1/5	-/-	0/4	2/4	3/3	0/5	0/5					

BMI: body mass index; ASA: American Society of Anesthesiologists.
Est1.: Chi-square, λ: Simmetric Goodman and Kruskal Lambda, τ.: Hospital independent Goodman and Kruskal Tau. K-W: Chi-Square Kruskal-Wallis, df: degrees of freedom. (P-V): P-value. ¥ statistically significant value.

Table 3: Technical aspects and results of surgery and analysis according to surgeons' experience

	N	Mean	n (%)	Confidence Interval 95%	Non-experienced surgeons (n = 24) N (%)	Experienced surgeons (n = 15) N (%)
Use of cystoscope*	27		2 (7.4)	(0.0 -17.3)	2 (16.7)	
Ureteral meatus access	35					
Direct			33 (94.3)	(86.6 -100)	18 (90.0)	15 (100.0)
Guidewire			2 (5.7)	(0.0 -13.4)	2 (10.0)	0 (0.0)
Dilatation			0 (0.0)		0 (0.0)	0 (0.0)
Use of "conventional" URS	39		4 (10.3)	(0.8 -19.8)	3 (12.5)	1 (6.7)
Stone fragmentation	39		35 (89.7)	(80.2 -99.2)	21 (87.5)	14 (93.3)
Upper stone migration	37		0 (0)		0 (0)	0 (0)
Operative time (minutes)	39	35.8		(29.3 -42.2)	31.1	43.3
Postoperative stent	35					
None			24 (68.6)	(53.2 -84.0)	15 (75.0)	9 (60.0)
External straight stent			5 (14.3)	(2.7 -25.9)	3 (15.0)	2 (13.3)
Double J stent			6 (17.1)	(4.7 -29.6)	2 (10.0)	4 (26.7)
Total time of stenting (days)	39	3.5		(1.5 -5.4)	3.2	3.9
Clavien -Dindo scale	39					
0			38 (97.4)	(92.4 -100.0)	23 (95.8)	15 (100.0)
I			0 (0)		0 (0.0)	0 (0.0)
II			1 (2.6)	(0.0 -7.6)	1 (4.2)	0 (0.0)
PULS	39					
0			30 (76.9)	(63.7 -90.1)	20 (83.3)	10 (66.7)
1			8 (20.5)	(7.8 -33.2)	3 (12.5)	5 (3.33)
2			1 (2.6)	(0.0 -7.6)	1 (4.2)	0 (0.0)
Inmediate stone-free status	34		30 (88.2)	(77.4 -99.1)	15 (79.9)	15 (100.0)

*Measures calculated on the number of patients not previously carrying a double J stent. URS: ureteroscope; PULS: post-ureteroscopic lesion scale.

Quantitative variables are expressed as mean and 95% confidence interval (95%), while qualitative do in frequency and percentage (%).

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10.1089/end.2016.0503)

Table 4: Technical aspects and results of the surgery in each center

Hospital	A	B	C	D	E	F	G	H	X^2/gl (P-V)	λ (P-V)	τ (P-V)	K-W/gl (P-V)	ANOVA (P-V)
Use of cystoscope *	0/5	2/4	0/5	-/-	0/2	0/1	0/5	0/5	12.4/6 0.053	0.083 0.524	0.460 0.063		
Ureteral meatus access													
Direct	5/5	4/5	5/5	-/-	4/5	5/5	5/5	5/5	5.30/6 0.506	0.031 0.310	0.152 0.525		
Guidewire	0/5	1/5	0/5	-/-	1/5	0/5	0/5	0/5					
Dilatation	0/5	0/5	0/5	-/-	0/5	0/5	0/5	0/5					
Use of "conventional" URS	0/5	0/5	1/5	2/4	0/5	1/5	0/5	0/5	10.7/7 0.150	0.5 0.525	0.28 0.163		
Stone fragmentation	5/5	5/5	5/5	3/4	4/5	4/5	5/5	4/5	4.8/7 0.687	0.03 0.311	0.12 0.507		
Operative time in minutes (median)	37	45	60	31	40	15	20	50				10.7/7 0.154	1.63 0.163
Upper stone migration	0/5	0/5	0/5	0/4	0/5	0/5	0/5	0/5	-	-	-		
Postoperative stent													
None	3/5	3/5	2/5	-/-	4/5	5/5	3/5	4/5	16.33/18 0.569	0.098 0.277	0.154 0.610		
External straight stent	0/5	1/5	1/5	-/-	1/5	0/5	1/5	1/5					
Double J stent	2/5	1/5	2/5	-/-	0/5	0/5	1/5	0/5					
Total time of stenting (days) (median)**	11	5.5	15	14	1	-	4	1				7.18/7 0.305	1.58 0.268
Clavien -Dindo scale													
0	5/5	5/5	5/5	4/4	4/5	5/5	5/5	5/5	7.0/7 0.431	0.03 0.311	0.18 0.450		
I	0/5	0/5	0/5	0/4	0/5	0/5	0/5	0/5					
II	0/5	0/5	0/5	0/4	1/5	0/5	0/5	0/5					
PULS													
0	4/5	4/5	3/5	4/4	3/5	4/5	5/5	3/5	13.7/14 0.476	0.07 0.401	0.16 0.604		
1	1/5	1/5	2/5	0/4	2/5	0/5	0/5	2/5					
2	0/5	0/5	0/5	0/4	0/5	1/5	0/5	0/5					
Inmediate stone-free status	5/5	4/5	5/5	4/4	4/5	-/-	3/5	5/5	7.03/6 0.318	0.061 0.145	0.207 0.338		

* Measures calculated among patients not previously carrying a double J stent. **Median calculated among patients with a postoperative stent in each center. URS: ureteroscope; PULS: post-ureteroscopic lesion scale.
Est1.: Chi-square, λ: Simmetric Goodman and Kruskal Lambda, τ.: Hospital independent Goodman and Kruskal Tau. K-W: Chi-Square Kruskal-Wallis, df: degrees of freedom. (P-V): P-value. ¥ Statistically significant value.